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EL596839631US

11-20-00

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: Ashvin H. Desai
Title: **METHOD FOR TISSUE TREATMENT WITH INJECTED SUBSTANCE**
Serial No.: CIP of 09/510,537 Filed February 22, 2000
Our File: 10284-0269451

TRANSMITTAL FOR NEW PATENT APPLICATION

Box Patent Application
Assistant Commissioner for Patents
Washington, D.C. 20231

Re: Continuation-in-Part Application

Sir:

Enclosed is a new patent application, including:

1. New Application Transmittal (16 pages);
2. Patent application, including 13-page specification, 6 pages of claims, 1-page abstract and 9 sheets of informal drawing;
3. Declaration and Power of Attorney (1 page); (unsigned)
4. Copy of Notification of Continuation Application filed in the parent case; and
5. Postcard for date-stamped confirmation of Patent Office's receipt of these materials.

This is an application filed pursuant to 37 CFR 1.53, permitting receipt of a filing date upon filing of specification, claims and drawings, if required, with applicant being given a period of one month from the date of notice to file the fee and oath or declaration.

Respectfully submitted,

David H. Jaffer
Reg. No. 32,243

Dated: November 17, 2000

PILLSBURY MADISON & SUTRO LLP
2550 Hanover Street
Palo Alto, CA 94304-1115
Telephone: (650) 233-4510
Facsimile: (650) 233-4545

CERTIFICATION UNDER 37 C.F.R. 1.10

I hereby certify that this correspondence and the documents referred to as attached hereto are being deposited with the United States Postal Service on this date November 17, 2000, in an envelope as "Express Mail Post Office to Addressee," mailing Label Number EL596839631US, addressed to the Assistant Commissioner for Patents, Washington, D.C. 20231.

Diana Dearing

Practitioner's Docket No. 10284-0269451 ***PATENT***

Preliminary Classification:

Proposed Class:

Subclass:

NOTE: "All applicants are requested to include a preliminary classification on newly filed patent applications. The preliminary classification, preferably class and subclass designations, should be identified in the upper right-hand corner of the letter of transmittal accompanying the application papers, for example 'Proposed Class 2, subclass 129.'" M.P.E.P. § 601, 7th ed.

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Box Patent Application
Assistant Commissioner for Patents
Washington, D.C. 20231

NEW APPLICATION TRANSMITTAL

Transmitted herewith for filing is the patent application of

Inventor(s): Ashvin H. Desai

WARNING: *37 C.F.R. § 1.41(a)(1) points out:*

"(a) A patent is applied for in the name or names of the actual inventor or inventors.

"(1) The inventorship of a nonprovisional application is that inventorship set forth in the oath or declaration as prescribed by § 1.63, except as provided for in § 1.53(d)(4) and § 1.63(d). If an oath or declaration as prescribed by § 1.63 is not filed during the pendency of a nonprovisional application, the inventorship is that inventorship set forth in the application papers filed pursuant to § 1.53(b), unless a petition under this paragraph accompanied by the fee set forth in § 1.17(i) is filed supplying or changing the name or names of the inventor or inventors."

For (title): METHOD FOR TISSUE TREATMENT WITH INJECTED SUBSTANCE

CERTIFICATION UNDER 37 C.F.R. § 1.10*
(Express Mail label number is mandatory.)
(Express Mail certification is optional.)

I hereby certify that this New Application Transmittal and the documents referred to as attached therein are being deposited with the United States Postal Service on this date _____, in an envelope as "Express Mail Post Office to Addressee," mailing Label Number EL596839631US, addressed to the: Assistant Commissioner for Patents, Washington, D.C. 20231.

Diana Dearing
(type or print name of person mailing paper)

Diana Dearing
Signature of person mailing paper

WARNING: *Certificate of mailing (first class) or facsimile transmission procedures of 37 C.F.R. § 1.8 cannot be used to obtain a date of mailing or transmission for this correspondence.*

***WARNING:** Each paper or fee filed by "Express Mail" **must** have the number of the "Express Mail" mailing label placed thereon prior to mailing. 37 C.F.R. § 1.10(b).*
*"Since the filing of correspondence under § 1.10 without the Express Mail mailing label thereon is an oversight that can be avoided by the exercise of reasonable care, requests for waiver of this requirement will **not** be granted on petition." Notice of Oct. 24, 1996, 60 Fed. Reg. 56,439, at 56,442.*

1. Type of Application

This new application is for a(n)

(check one applicable item below)

☐ Original (nonprovisional)

☐ Design

☐ Plant

WARNING: ***Do not*** *use this transmittal for a completion in the U.S. of an International Application under 35 U.S.C. § 371(c)(4), unless the International Application is being filed as a divisional, continuation or continuation-in-part application.*

WARNING: ***Do not*** *use this transmittal for the filing of a provisional application.*

NOTE: If one of the following 3 items apply, then complete and attach ADDED PAGES FOR NEW APPLICATION TRANSMITTAL WHERE BENEFIT OF A PRIOR U.S. APPLICATION CLAIMED and a NOTIFICATION IN PARENT APPLICATION OF THE FILING OF THIS CONTINUATION APPLICATION.

☐ Divisional.

☐ Continuation.

☒ Continuation-in-part (C-I-P).

2. Benefit of Prior U.S. Application(s) (35 U.S.C. §§ 119(e), 120, or 121)

NOTE: A nonprovisional application may claim an invention disclosed in one or more prior filed copending nonprovisional applications or copending international applications designating the United States of America. In order for a nonprovisional application to claim the benefit of a prior filed copending nonprovisional application or copending international application designating the United States of America, each prior application must name as an inventor at least one inventor named in the later filed nonprovisional application and disclose the named inventor's invention claimed in at least one claim of the later filed nonprovisional application in the manner provided by the first paragraph of 35 U.S.C. § 112. Each prior application must also be:

(i) An international application entitled to a filing date in accordance with PCT Article 11 and designating the United States of America; or

(ii) Complete as set forth in § 1.51(b); or

(iii) Entitled to a filing date as set forth in § 1.53(b) or § 1.53(d) and include the basic filing fee set forth in § 1.16; or

(iv) Entitled to a filing date as set forth in § 1.53(b) and have paid therein the processing and retention fee set forth in § 1.21(l) within the time period set forth in § 1.53(f).

37 C.F.R. § 1.78(a)(1).

NOTE: If the new application being transmitted is a divisional, continuation or a continuation-in-part of a parent case, or where the parent case is an International Application which designated the U.S., or benefit of a prior provisional application is claimed, then check the following item and complete and attach ADDED PAGES FOR NEW APPLICATION TRANSMITTAL WHERE BENEFIT OF PRIOR U.S. APPLICATION(S) CLAIMED.

WARNING: *If an application claims the benefit of the filing date of an earlier filed application under 35 U.S.C. §§ 120, 121 or 365(c), the 20-year term of that application will be based upon the filing date of the earliest U.S. application that the application makes reference to under 35 U.S.C. §§ 120, 121 or 365(c). (35 U.S.C. § 154(a)(2) does not take into account, for the determination of the patent term, any application on which priority is claimed under 35 U.S.C. §§ 119, 365(a) or 365(b).) For a c-i-p application, applicant should review whether any claim in the patent that will issue is supported by an earlier application and, if not, the applicant should consider canceling the reference to the earlier filed application. The term of a patent is not based on a claim-by-claim approach. See Notice of April 14, 1995, 60 Fed. Reg. 20,195, at 20,205.*

WARNING: *When the last day of pendency of a provisional application falls on a Saturday, Sunday, or Federal holiday within the District of Columbia, any nonprovisional application claiming benefit of the provisional application* ***must*** *be filed prior to the Saturday, Sunday, or Federal holiday within the District of Columbia. See 37 C.F.R. § 1.78(a)(3).*

☒ The new application being transmitted claims the benefit of prior U.S. application(s). Enclosed are ADDED PAGES FOR NEW APPLICATION TRANSMITTAL WHERE BENEFIT OF PRIOR U.S. APPLICATION(S) CLAIMED.

3. Papers Enclosed

A. Required for filing date under 37 C.F.R. § 1.53(b) (Regular) or 37 C.F.R. § 1.153 (Design) Application

13 Pages of specification

6 Pages of claims

9 Sheets of drawing

WARNING: ***DO NOT*** *submit original drawings. A high quality copy of the drawings should be supplied when filing a patent application. The drawings that are submitted to the Office must be on strong, white, smooth, and non-shiny paper and meet the standards according to § 1.84. If corrections to the drawings are necessary, they should be made to the original drawing and a high-quality copy of the corrected original drawing then submitted to the Office. Only one copy is required or desired. For comments on proposed then-new 37 C.F.R. § 1.84, see Notice of March 9, 1988 (1990 O.G. 57-62).*

NOTE: "Identifying indicia, if provided, should include the application number or the title of the invention, inventor's name, docket number (if any), and the name and telephone number of a person to call if the Office is unable to match the drawings to the proper application. This information should be placed on the back of each sheet of drawing a minimum distance of 1.5 cm. (5/8 inch) down from the top of the page . . ." 37 C.F.R. § 1.84(c)).

(complete the following, if applicable)

☐ The enclosed drawing(s) are photograph(s), and there is also attached a "PETITION TO ACCEPT PHOTOGRAPH(S) AS DRAWING(S)." 37 C.F.R. § 1.84(b).

☐ formal

☒ informal

B. Other Papers Enclosed

____ Pages of declaration and power of attorney

1 Pages of abstract

____ Other

4. Additional papers enclosed

☐ Amendment to claims

☐ Cancel in this applications claims _____ before calculating the filing fee. (At least one original independent claim must be retained for filing purposes.)

☐ Add the claims shown on the attached amendment. (Claims added have been numbered consecutively following the highest numbered original claims.)

☐ Preliminary Amendment

☐ Information Disclosure Statement (37 C.F.R. § 1.98)

☐ Form PTO–1449 (PTO/SB/08A and 08B)

☐ Citations

☐ Declaration of Biological Deposit

☐ Submission of "Sequence Listing," computer readable copy and/or amendment pertaining thereto for biotechnology invention containing nucleotide and/or amino acid sequence.

☐ Authorization of Attorney(s) to Accept and Follow Instructions from Representative

☐ Special Comments

☐ Other

5. Declaration or oath (including power of attorney)

NOTE: A newly executed declaration is not required in a continuation or divisional application provided that the prior nonprovisional application contained a declaration as required, the application being filed is by all or fewer than all the inventors named in the prior application, there is no new matter in the application being filed, and a copy of the executed declaration filed in the prior application (showing the signature or an indication thereon that it was signed) is submitted. The copy must be accompanied by a statement requesting deletion of the names of person(s) who are not inventors of the application being filed. If the declaration in the prior application was filed under § 1.47, then a copy of that declaration must be filed accompanied by a copy of the decision granting § 1.47 status or, if a nonsigning person under § 1.47 has subsequently joined in a prior application, then a copy of the subsequently executed declaration must be filed. See 37 C.F.R. §§ 1.63(d)(1)-(3).

NOTE: A declaration filed to complete an application must be executed, identify the specification to which it is directed, identify each inventor by full name including family name and at least one given name, without abbreviation together with any other given name or initial, and the residence, post office address and country or citizenship of each inventor, and state whether the inventor is a sole or joint inventor. 37 C.F.R. § 1.63(a)(1)-(4).

NOTE: "The inventorship of a nonprovisional application is that inventorship set forth in the oath or declaration as prescribed by § 1.62, except as provided for in § 1.53(d)(4) and § 1.63(d). If an oath or declaration as prescribed by § 1.63 is not filed during the pendency of a nonprovisional application, the inventorship is that inventorship set forth in the application papers filed pursuant to § 1.53(b), unless a petition under this paragraph accompanied by the fee set forth in § 1.17(i) is filed supplying or changing the name or names of the inventor or inventors." 37 C.F.R. § 1.41(a)(1).

☑ Enclosed

Executed by

(check **all** *applicable boxes)*

☑ inventor(s). (unsigned)

☐ legal representative of inventor(s). 37 C.F.R. §§ 1.42 or 1.43.

☐ joint inventor or person showing a proprietary interest on behalf of inventor who refused to sign or cannot be reached.

☐ This is the petition required by 37 C.F.R. § 1.47 and the statement required by 37 C.F.R. § 1.47 is also attached. See item 13 below for fee.

☒ Not Enclosed.

NOTE: Where the filing is a completion in the U.S. of an International Application or where the completion of the U.S. application contains subject matter in addition to the International Application, the application may be treated as a continuation or continuation-in-part, as the case may be, utilizing ADDED PAGE FOR NEW APPLICATION TRANSMITTAL WHERE BENEFIT OF PRIOR U.S. APPLICATION CLAIMED.

☐ Application is made by a person authorized under 37 C.F.R. § 1.41(c) on behalf of *all* the above named inventor(s).

(The declaration or oath, along with the surcharge required by 37 C.F.R. § 1.16(e) can be filed subsequently).

☐ Showing that the filing is authorized.
(not required unless called into question. 37 C.F.R. § 1.41(d))

6. Inventorship Statement

WARNING: *If the named inventors are each not the inventors of all the claims an explanation, including the ownership of the various claims at the time the last claimed invention was made, should be submitted.*

The inventorship for all the claims in this application are:

☒ The same.

or

☐ Not the same. An explanation, including the ownership of the various claims at the time the last claimed invention was made,

☐ is submitted.

☐ will be submitted.

7. Language

NOTE: An application including a signed oath or declaration may be filed in a language other than English. An English translation of the non-English language application and the processing fee of $130.00 required by 37 C.F.R. § 1.17(k) is required to be filed with the application, or within such time as may be set by the Office. 37 C.F.R. § 1.52(d).

☒ English

☐ Non-English

☐ The attached translation includes a statement that the translation is accurate. 37 C.F.R. § 1.52(d).

8. Assignment

☐ An assignment of the invention to _____

_____

☐ is attached. A separate ☐ "COVER SHEET FOR ASSIGNMENT (DOCUMENT) ACCOMPANYING NEW PATENT APPLICATION" or ☐ FORM PTO 1595 is also attached.

☐ will follow.

NOTE: "If an assignment is submitted with a new application, send two separate letters-one for the application and one for the assignment." Notice of May 4, 1990 (1114 O.G. 77-78).

WARNING: *A newly executed "CERTIFICATE UNDER 37 C.F.R. § 3.73(b)" must be filed when a continuation-in-part application is filed by an assignee. Notice of April 30, 1993, 1150 O.G. 62-64.*

9. Certified Copy

Certified copy(ies) of application(s)

Country	Appln. No.	Filed
Country	Appln. No.	Filed
Country	Appln. No.	Filed

from which priority is claimed

☐ is (are) attached.

☐ will follow.

NOTE: The foreign application forming the basis for the claim for priority must be referred to in the oath or declaration. 37 C.F.R. § 1.55(a) and 1.63.

NOTE: This item is for any foreign priority for which the application being filed directly relates. If any parent U.S. application or International Application from which this application claims benefit under 35 U.S.C. § 120 is itself entitled to priority from a prior foreign application, then complete item 18 on the ADDED PAGES FOR NEW APPLICATION TRANSMITTAL WHERE BENEFIT OF PRIOR U.S. APPLICATION(S) CLAIMED.

10. Fee Calculation (37 C.F.R. § 1.16)

A. ☒ Regular application

CLAIMS AS FILED				
	Number filed	Number Extra	Rate	Basic Fee 37 C.F.R. § 1.16(a) ~~$690.00~~ 710.00
Total Claims (37 C.F.R. § 1.16(c))	41	− 20 = 21	× $ 18.00	$378.00
Independent Claims (37 C.F.R. § 1.16(b))	2	− 3 = 0	× $ 78.00	
Multiple dependent claim(s), if any (37 C.F.R. § 1.16(d))			+ $260.00	

☐ Amendment cancelling extra claims is enclosed.

☐ Amendment deleting multiple-dependencies is enclosed.

☐ Fee for extra claims is not being paid at this time.

NOTE: If the fees for extra claims are not paid on filing they must be paid or the claims cancelled by amendment, prior to the expiration of the time period set for response by the Patent and Trademark Office in any notice of fee deficiency. 37 C.F.R. § 1.16(d).

Filing Fee Calculation $ 1,088.00

B. ☐ Design application ($310.00—37 C.F.R. § 1.16(f))

Filing Fee Calculation $_____

C. ☐ Plant application
($480.00—37 C.F.R. § 1.16(g))

Filing fee calculation $_____

11. Small Entity Statement(s)

☐ Statement(s) that this is a filing by a small entity under 37 C.F.R. § 1.9 and 1.27 is (are) attached.

WARNING: *"Status as a small entity must be specifically established in each application or patent in which the status is available and desired. Status as a small entity in one application or patent does not affect any other application or patent, including applications or patents which are directly or indirectly dependent upon the application or patent in which the status has been established. The refiling of an application under § 1.53 as a continuation, division, or continuation-in-part (including a continued prosecution application under § 1.53(d)), or the filing of a reissue application requires a new determination as to continued entitlement to small entity status for the continuing or reissue application. A nonprovisional application claiming benefit under 35 U.S.C. § 119(e), 120, 121, or 365(c) of a prior application, or a reissue application may rely on a statement filed in the prior application or in the patent if the nonprovisional application or the reissue application includes a reference to the statement in the prior application or in the patent or includes a copy of the statement in the prior application or in the patent and status as a small entity is still proper and desired. The payment of the small entity basic statutory filing fee will be treated as such a reference for purposes of this section." 37 C.F.R. § 1.28(a)(2).*

WARNING: *"Small entity status must not be established when the person or persons signing the . . . statement can **unequivocally** make the required self-certification." M.P.E.P., § 509.03, 6th ed., rev. 2, July 1996 (emphasis added).*

(complete the following, if applicable)

☐ Status as a small entity was claimed in prior application

_____ / _____, filed on _____, from which benefit is being claimed for this application under:

35 U.S.C. § ☐ 119(e),
☐ 120,
☐ 121,
☐ 365(c),

and which status as a small entity is still proper and desired.

☐ A copy of the statement in the prior application is included.

Filing Fee Calculation (50% of **A, B** or **C** above)

$_____

NOTE: Any excess of the full fee paid will be refunded if small entitiy status is established and a refund request are filed within 2 months of the date of timely payment of a full fee. The two-month period is not extendable under § 1.136. 37 C.F.R. § 1.28(a).

12. Request for International-Type Search (37 C.F.R. § 1.104(d))

(complete, if applicable)

☐ Please prepare an international-type search report for this application at the time when national examination on the merits takes place.

13. Fee Payment Being Made at This Time

☒ Not Enclosed

☒ No filing fee is to be paid at this time.
(This and the surcharge required by 37 C.F.R. § 1.16(e) can be paid subsequently.)

☐ Enclosed

☐ Filing fee $ _____

☐ Recording assignment ($40.00; 37 C.F.R. § 1.21(h)) (See attached "COVER SHEET FOR ASSIGNMENT ACCOMPANYING NEW APPLICATION".) $ _____

☐ Petition fee for filing by other than all the inventors or person on behalf of the inventor where inventor refused to sign or cannot be reached ($130.00; 37 C.F.R. §§ 1.47 and 1.17(i)) $ _____

☐ For processing an application with a specification in a non-English language ($130.00; 37 C.F.R. §§ 1.52(d) and 1.17(k)) $ _____

☐ Processing and retention fee ($130.00; 37 C.F.R. §§ 1.53(d) and 1.21(l)) $ _____

☐ Fee for international-type search report ($40.00; 37 C.F.R. § 1.21(e)) $ _____

NOTE: 37 C.F.R. § 1.21(l) establishes a fee for processing and retaining any application that is abandoned for failing to complete the application pursuant to 37 C.F.R. § 1.53(f) and this, as well as the changes to 37 C.F.R. §§ 1.53 and 1.78(a)(1), indicate that in order to obtain the benefit of a prior U.S. application, either the basic filing fee must be paid, or the processing and retention fee of § 1.21(l) must be paid, within 1 year from notification under § 53(f).

Total fees enclosed $_____

14. Method of Payment of Fees

☐ Check in the amount of $_____

☐ Charge Account No. _____ in the amount of $_____.

A duplicate of this transmittal is attached.

NOTE: Fees should be itemized in such a manner that it is clear for which purpose the fees are paid. 37 C.F.R. § 1.22(b).

15. Authorization to Charge Additional Fees

WARNING: *If no fees are to be paid on filing, the following items should not be completed.*

WARNING: *Accurately count claims, especially multiple dependent claims, to avoid unexpected high charges, if extra claim charges are authorized.*

☐ The Commissioner is hereby authorized to charge the following additional fees by this paper and during the entire pendency of this application to Account No. _____:

☐ 37 C.F.R. § 1.16(a), (f) or (g) (filing fees)

☐ 37 C.F.R. § 1.16(b), (c) and (d) (presentation of extra claims)

NOTE: Because additional fees for excess or multiple dependent claims not paid on filing or on later presentation must only be paid or these claims cancelled by amendment prior to the expiration of the time period set for response by the PTO in any notice of fee deficiency (37 C.F.R. § 1.16(d)), it might be best not to authonze the PTO to charge additional claim fees, except possibly when dealing with amendments after final action.

☐ 37 C.F.R. § 1.16(e) (surcharge for filing the basic filing fee and/or declaration on a date later than the filing date of the application)

☐ 37 C.F.R. § 1.17(a)(1)–(5) (extension fees pursuant to § 1.136(a)).

☐ 37 C.F.R. § 1.17 (application processing fees)

NOTE: ". . .A written request may be submitted in an application that is an authorization to treat any concurrent or future reply, requiring a petition for an extension of time under this paragraph for its timely submission, as incorporating a petition for extension of time for the appropriate length of time. An authorization to charge all required fees, fees under § 1.17, or all required extension of time fees will be treated as a constructive petition for an extension of time in any concurrent or future reply requiring a petition for an extension of time under this paragraph for its timely submission. Submission of the fee set forth in § 1.17(a) will also be treated as a constructive petition for an extension of time in any concurrent reply requiring a petition for an extension of time under this paragraph for its timely submission." 37 C.F.R. § 1.136(a)(3).

☐ 37 C.F.R. § 1.18 (issue fee at or before mailing of Notice of Allowance, pursuant to 37 C.F.R. § 1.311(b))

NOTE: Where an authorization to charge the issue fee to a deposit account has been filed before the mailing of a Notice of Allowance, the issue fee will be automatically charged to the deposit account at the time of mailing the notice of allowance. 37 C.F.R. § 1.311(b).

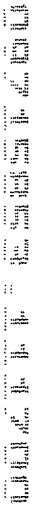
NOTE: 37 C.F.R. § 1.28(b) requires "Notification of any change in status resulting in loss of entitlement to small entity status must be filed in the application . . . prior to paying, or at the time of paying, . . . the issue fee. . . " From the wording of 37 C.F.R. § 1.28(b), (a) notification of change of status must be made even if the fee is paid as "other than a small entity" and (b) no notification is required if the change is to another small entity.

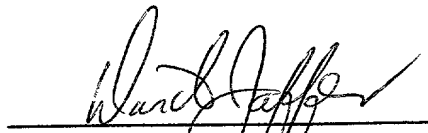
16. Instructions as to Overpayment

NOTE: ". . . Amounts of twenty-five dollars or less will not be returned unless specifically requested within a reasonable time, nor will the payer be notified of such amounts; amounts over twenty-five dollars may be returned by check or, if requested, by credit to a deposit account." 37 C.F.R. § 1.26(a).

☐ Credit Account No. _____

☐ Refund





SIGNATURE OF PRACTITIONER

David H. Jaffer

PILLSBURY MADISON & SUTRO LLP

(type or print name of attorney)

2550 Hanover Street

Palo Alto, CA 94304-1115

P.O. Address

Reg. No. 32,243

Tel. No. (650)233-4500

Customer No. 24729

(New Application Transmittal [4-1]—page 10 of 11)

☒ **Incorporation by reference of added pages**

(check the following item if the application in this transmittal claims the benefit of prior U.S. application(s) (including an international application entering the U.S. stage as a continuation, divisional or C-I-P application) and complete and attach the ADDED PAGES FOR NEW APPLICATION TRANSMITTAL WHERE BENEFIT OF PRIOR U.S. APPLICATION(S) CLAIMED)

☒ Plus Added Pages for New Application Transmittal Where Benefit of Prior U.S. Application(s) Claimed

Number of pages added 5

☐ Plus Added Pages for Papers Referred to in Item 4 Above

Number of pages added _____

☐ Plus added pages deleting names of inventor(s) named in prior application(s) who is/are no longer inventor(s) of the subject matter claimed in this application.

Number of pages added _____

☐ Plus "Assignment Cover Letter Accompanying New Application"

Number of pages added _____

☐ **Statement Where No Further Pages Added**

(if no further pages form a part of this Transmittal, then end this Transmittal with this page and check the following item)

☐ This transmittal ends with this page.

Practitioner's Docket No. 10284-0269451 ***PATENT***

ADDED PAGES FOR APPLICATION TRANSMITTAL WHERE BENEFIT OF PRIOR U.S. APPLICATION(S) CLAIMED

NOTE: See 37 C.F.R. § 1.78.

17. Relate Back

WARNING: *If an application claims the benefit of the filing date of an earlier filed application under 35 U.S.C. §§ 120, 121 or 365(c), the 20-year term of that application will be based upon the filing date of the earliest U.S. application that the application makes reference to under 35 U.S.C. §§ 120, 121 or 365(c). (35 U.S.C. § 154(a)(2) does not take into account, for the determination of the patent term, any application on which priority is claimed under 35 U.S.C. §§ 119, 365(a) or 365(b).) For a c-i-p application, applicant should review whether any claim in the patent that will issue is supported by an earlier application and, if not, the applicant should consider canceling the reference to the earlier filed application. The term of a patent is not based on a claim-by-claim approach. See Notice of April 14, 1995, 60 Fed. Reg. 20,195, at 20,205.*

(complete the following, if applicable)

☐ Amend the specification by inserting, before the first line, the following sentence:

A. 35 U.S.C. § 119(e)

NOTE: "Any nonprovisional application claiming the benefit of one or more prior filed copending provisional applications must contain or be amended to contain in the first sentence of the specification following the title a reference to each such prior provisional application, identifying it as a provisional application, and including the provisional application number (consisting of series code and serial number)." 37 C.F.R. § 1.78(a)(4).

☐ "This application claims the benefit of U.S. Provisional Application(s) No(s).:

APPLICATION NO(S).:	FILING DATE
_____ /_____	_____ "
_____ /_____	_____ "
_____ /_____	_____ "

B. 35 U.S.C. §§ 120, 121 and 365(c)

NOTE: "Except for a continued prosecution application filed under § 1.53(d), any nonprovisional application claiming the benefit of one or more prior filed copending nonprovisional applications or international applications designating the United States of America must contain or be amended to contain in the first sentence of the specification following the title a reference to each such prior application, identifying it by application number (consisting of the series code and serial number) or international application number and international filing date and indicating the relationship of the applications. . . . Cross-references to other related applications may be made when appropriate." (See § 1.14(a)). 37 C.F.R. § 1.78(a)(2).

☒ "This application is a CIP of 09/519,937, filed 3-22-00, which is a CIP of 09/105,896, filed 6-26-98 [redacted], which is a CIP of 08/639,199, filed 4-26-96 (now 5,861,002), which is a CIP of 08/259,712, filed 6-14-94 (now 5,562,703), which is a CIP of 08/025,003, filed 3-2-93 (abandoned), which is a cont. of 07/779,108, filed 10-18-91 (now 5,322,503).

- ☐ continuation
- ☒ continuation-in-part
- ☐ divisional

of copending application(s)

☒ application number 0 /_____ filed on _____"

☐ International Application _____ filed on _____ and which designated the U.S."

NOTE: The proper reference to a prior filed PCT application that entered the U.S. national phase is the U.S. serial number and the filing date of the PCT application that designated the U.S.

NOTE: (1) Where the application being transmitted adds subject matter to the International Application, then the filing can be as a continuation-in-part or (2) if it is desired to do so for other reasons then the filing can be as a continuation.

NOTE: The deadline for entering the national phase in the U.S. for an international application was clarified in the Notice of April 28, 1987 (1079 O.G. 32 to 46) as follows:

"The Patent and Trademark Office considers the international application to be pending until the 22nd month from the priority date if the United States has been designated and no Demand for International Preliminary Examination has been filed prior to the expiration of the 19th month from the priority date and until the 32nd month from the priority date if a Demand for International Preliminary Examination which elected the United States of America has been filed prior to the expiration of the 19th month from the priority date, provided that a copy of the international application has been communicated to the Patent and Trademark Office within the 20 or 30 month period respectively. If a copy of the international application has not been communicated to the Patent and Trademark Office within the 20 or 30 month period respectively, the international application becomes abandoned as to the United States 20 or 30 months from the priority date respectivley. These periods have been placed in the rules as paragraph (h) of § 1.494 and paragraph (i) of § 1.495. A continuing application under 35 U.S.C. 365(c) and 120 may be filed anytime during the pendency of the international application."

☐ "The nonprovisional application designated above, namely application _____ / _____, filed _____, claims the benefit of U.S. Provisional Application(s) No(s).:

APPLICATION NO(S).:	FILING DATE
_____ /_____	_____"
_____ /_____	_____"
_____ /_____	_____"

☐ Where more than one reference is made above, please combine all references into one sentence.

18. Relate Back—35 U.S.C. § 119 Priority Claim for Prior Application

The prior U.S. application(s), including any prior International Application designating the U.S., identified above in Item 17B, in turn itself claim(s) foreign priority(ies) as follows:

Country	Appln. no.	Filed on

The certified copy(ies) has (have)

☐ been filed on _____, in prior application 0 /_____, which was filed on _____.

☐ is (are) attached.

WARNING: *The certified copy of the priority application that may have been communicated to the PTO by the International Bureau may **not** be relied on without any need to file a certified copy of the priority application **in the continuing application.** This is so because the certified copy of the priority application communicated by the International Bureau is placed in a folder and is not assigned a U.S. serial number unless the national stage is entered. Such folders are disposed of if the national stage is not entered. Therefore, such certified copies may not be available if needed later in the prosecution of a continuing application. An alternative would be to physically remove the priority documents from the folders and transfer them to the continuing application. The resources required to request transfer, retrieve the folders, make suitable record notations, transfer the certified copies, enter and make a record of such copies in the Continuing Application are substantial. Accordingly, the priority documents in folders of international applications that have not entered the national stage may not be relied on. Notice of April 28, 1987 (1079 O.G. 32 to 46).*

19. Maintenance of Copendency of Prior Application

NOTE: The PTO finds it useful if a copy of the petition filed in the prior application extending the term for response is filed with the papers constituting the filing of the continuation application. Notice of November 5, 1985 (1060 O.G. 27).

A. ☐ Extension of time in prior application

*(This item **must** be completed and the papers filed **in the prior application,** if the period set in the prior application has run.)*

☐ A petition, fee and response extends the term in the pending **prior** application until _____.

☐ A **copy** of the petition filed in prior application is attached.

B. ☐ Conditional Petition for Extension of Time in Prior Application

(complete this item, if previous item not applicable)

☐ A conditional petition for extension of time is being filed in the ~~pending~~ **prior** application.

☐ A **copy** of the conditional petition filed in the prior application is attached.

20. Further Inventorship Statement Where Benefit of Prior Application(s) Claimed

(complete applicable item (a), (b) and/or (c) below)

(a) ☐ This application discloses and claims only subject matter disclosed in the prior application whose particulars are set out above and the inventor(s) in this application are

- ☐ the same.
- ☐ less than those named in the prior application. It is requested that the following inventor(s) identified for the prior application be deleted:

_____

(type name(s) of inventor(s) to be deleted)

(b) ☒ This application discloses and claims additional disclosure by amendment and a new declaration or oath is being filed. With respect to the prior application, the inventor(s) in this application are

- ☒ the same.
- ☐ the following additional inventor(s) have been added:

_____

(type name(s) of inventor(s) to be added)

(c) The inventorship for all the claims in this application are

- ☒ the same.
- ☐ not the same. An explanation, including the ownership of the various claims at the time the last claimed invention was made
  - ☐ is submitted.
  - ☐ will be submitted.

21. Abandonment of Prior Application *(if applicable)*

☐ Please abandon the prior application at a time while the prior application is pending, or when the petition for extension of time or to revive in that application is granted, and when this application is granted a filing date, so as to make this application copending with said prior application.

NOTE: According to the Notice of May 13, 1983 (103, TMOG 6-7), the filing of a continuation or continuation-in-part application is a proper response with respect to a petition for extension of time or a petition to revive and should include the express abandonment of the prior application conditioned upon the granting of the petition and the granting of a filing date to the continuing application.

22. Petition for Suspension of Prosecution for the Time Necessary to File an Amendment

WARNING: *"The claims of a new application may be finally rejected in the first Office action in those situations where (A) the new application is a continuing application of, or a substitute for, an earlier application, and (B) all the claims of the new application (1) are drawn to the same invention claimed in the earlier application, and (2) would have been properly finally rejected on the grounds of art of record in the next Office action if they had been entered in the earlier application." M.P.E.P., § 706.07(b), 7th ed.*

NOTE: Where it is possible that the claims on file will give rise to a first action final for this continuation application and for some reason an amendment cannot be filed promptly (e.g., experimental data is being gathered) it may be desirable to file a petition for suspension of prosecution for the time necessary.

(check the next item, if applicable)

☐ There is provided herewith a Petition To Suspend Prosecution for the Time Necessary to File An Amendment (New Application Filed Concurrently)

23. Small Entity (37 C.F.R. § 1.28(a))

☐ Applicant has established small entity status by the filing of a statement in parent application /_____ on _____ .

☐ A copy of the statement previously filed is included.

WARNING: *See 37 C.F.R. § 1.28(a).*

WARNING: *"Small entity status must not be established when the person or persons signing the . . . statement can **unequivocally** make the required self-certification." M.P.E.P., § 509.03, 7th ed. (emphasis added).*

24. NOTIFICATION IN PARENT APPLICATION OF THIS FILING

☒ A notification of the filing of this
(check one of the following)

☐ continuation

☒ continuation-in-part

☐ divisional

is being filed in the parent application, from which this application claims priority under 35 U.S.C. § 120.

Practitioner's Docket No. 10284-0269451 **PATENT**

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of: Ashvin H. Desai
Application No.: 0 9 /510,537 Group No.:
Filed: February 22, 2000 Examiner:
For: METHOD FOR TISSUE TREATMENT WITH INJECTED SUBSTANCE

Assistant Commissioner for Patents
Washington, D.C. 20231

NOTIFICATION OF FILING OF CONTINUING, DIVISIONAL OR CONTINUED PROSECUTION APPLICATION

Notification is hereby being made of the filing of a:

- ☐ continuation
- ☒ continuation-in-part
- ☐ divisional
- ☐ continued prosecution

application for this case

- ☒ concurrently herewith.
- ☐ on _____ .
  Date

CERTIFICATION UNDER 37 C.F.R. §§ 1.8(a) and 1.10
(When using Express Mail, the Express Mail label number is mandatory; Express Mail certification is optional.)

I hereby certify that, on the date shown below, this correspondence is being:

MAILING

☒ deposited with the United States Postal Service in an envelope addressed to the Assistant Commissioner for Patents, Washington, D.C. 20231

37 C.F.R. § 1.8(a)

☐ with sufficient postage as first class mail.

37 C.F.R. § 1.10*

☒ as "Express Mail Post Office to Addressee" Mailing Label No. _____ **(mandatory)**

TRANSMISSION

☐ transmitted by facsimile to the Patent and Trademark Office.

Diana Dearing
Signature

Date: November 17, 2000

Diana Dearing
(type or print name of person certifying)

WARNING:** *Each paper or fee filed by Express Mail* ***must *have the number of the "Express Mail" mailing label placed thereon prior to mailing. 37 C.F.R. § 1.10(b).*
"Since the filing of correspondence under § 1.10 without the Express Mail mailing label thereon is an oversight that can be avoided by the exercise of reasonable care, requests for waiver of this requirement will ***not*** *be granted on petition." Notice of Oct. 24, 1996, 60 Fed. Reg. 56,439, at 56,442.*

SIGNATURE OF PRACTITIONER

Reg. No. 32,243

David H. Jaffer

(type or print name of practitioner)

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Specification

METHOD FOR TISSUE TREATMENT WITH INJECTED SUBSTANCE

Background of the Invention

Related Cases

This application is a Continuation-in-Part of copending U.S. Patent Application Serial No. 09/510,537 filed February 22, 2000 which is a Continuation-in-Part of copending U.S. Patent Application Serial No. 09/105,896 filed June 26, 1998.

Field of the Invention

The present invention relates generally to methods and apparatus for body tissue treatment using injection apparatus, and more particularly to a method wherein a treatment substance is injected in the form of a highly viscous material for retarding substance disbursement to cause selective tissue necrosis in a controlled area of treatment, and to enhance and localize the use of substances for tissue necrosis by injecting a conductive viscous material to act as an electrode extension with simultaneous application of radio frequency (RF) energy.

Description of the Prior Art

Various methods of treating diseased body tissue have been employed, including surgical removal, freezing and treatment with chemical agents and RF energy. A variety of treatment fluids are currently known to be of benefit in treating diseased tissue. For example, there are a number of tumor suppressor genes, viral vectors, markers, vaccines, enzymes, proteins and biological agents that can be used for gene therapy and cancer treatment. The current method of delivery of these substances is to inject them into the blood stream through use of a conventional needle and syringe. The result is that the substance is carried by the blood to every part of the body. In many cases, it would be advantageous to be able to treat only a particular organ, or part of an organ.

Attempts to destroy diseased tissue with RF energy are limited in success due in part to a lack of technology to cause larger tissue lesions using RF energy through small incisions in the body. A common technique of RF energy application known as "monopolar" mode applies RF

energy to large areas of healthy tissue as well as the diseased portion. In this case, a single RF input electrode is positioned near the diseased tissue, and a return electrode, usually in the form of a plate is positioned on the outside of the body. Application of RF energy in what is known as "bipolar" mode restricts the energy distribution, but requires precision placement of at least two electrodes.

The treatment of diseased tissue is aided by use of laparoscopic/endoscopic surgical instruments that allow a surgeon to see inside the body cavity of a patient without the necessity of large incisions. This reduces the chances of infection and other complications related to large incisions. The endoscope further allows the surgeon to manipulate microsurgical instruments without impeding the surgeon's view of the area under consideration. Although endoscopic surgical instruments are well developed and in use for surgical operations, an apparatus and method is not described or used in the prior art for delivering a treatment fluid interstitially to a precise target area within a body.

It is therefore apparent that there is a need for an improved method of treating diseased tissue, including an apparatus that can deliver a treatment fluid to an interior localized body area. There is also a need for a method providing greater control over the volume of tissue treated in the use of RF energy therapy.

SUMMARY OF THE INVENTION

It is therefore an object of the present invention to provide an improved method of treating a localized volume of body tissue.

It is a further object of the present invention to provide a method of localized tissue treatment by injecting a treatment substance in the form of a gel.

It is another object of the present invention to provide a method of tissue therapy including the injection of an electrically conductive substance for concentrating applied RF energy by effectively extending the range of an RF electrode.

It is a still further object of the present invention to provide a method of body tissue therapy wherein a needle is inserted through a biopsy needle guide for application of a

conductive treatment substance, and wherein RF energy is applied through an electrically conductive needle.

It is another object of the present invention to provide a method of injecting a specific treatment substance to a localized interior body part.

It is an object of the present invention to provide a method of applying a treatment substance to a localized body portion by guiding a needle with an endoscopic surgical instrument.

It is a further object of the present invention to provide a method of injecting a treatment substance to a localized body portion by guiding a needle through the body to the localized portion by use of a non-invasive imaging device.

Briefly, a preferred embodiment of the present invention includes a method wherein a viscous treatment substance is injected into a diseased portion of body tissue for the purpose of localized, selective necrosis of target tissue by resisting substance migration. The treatment substance injected is in the form of a gel, or alternatively in the form of microspheres. Localized treatment is further enhanced by including a conductive component in the treatment substance, and while injecting the substance, simultaneously applying RF (radio frequency) energy to an injection needle acting as an RF electrode. The conductive gel serves as an extension of the electrode, thereby localizing and enhancing treatment in the volume penetrated by the gel. Improved positioning of the injection needle is aided with the use of ultrasound imaging with clarity enhanced by inclusion of imaging enhancement agents in the gel. Alternatively, microspheres are filled with a gel/solution and gas combination providing contrasting areas of ultrasound reflection.

An advantage of the present invention is that it allows a lethal fluid to be injected into a tumor without seriously affecting the surrounding healthy tissue.

A further advantage of the present invention is that it provides a selective treatment of cancer cells, avoiding the need to inject toxic substances throughout a patient's body.

A still further advantage of the present invention is that it provides enhanced control of a volume of tissue being treated with substances and radio frequency energy.

Brief Description of the Drawings

Fig. 1a illustrates various organs that can be treated according to the present invention;

Fig. 1b shows transperineal injection for treating the prostate;

Fig. 2 shows a microsphere;

Fig. 3 illustrates various alternate methods of treatment of an organ, showing treatment of a prostate;

Fig. 4 illustrates transurethral treatment of a prostate;

Fig. 5 illustrates a biopsy apparatus as used in the present invention, and as applied to treatment of a breast;

Fig. 6 illustrates various components of a gel;

Fig. 7 is a list of therapy substances;

Fig. 8 is a list of electrically conductive material for use in a gel, or in a microsphere;

Fig. 9 is a list of binding/gelling agents;

Fig. 10 lists image contrast agents;

Fig. 11 illustrates components of a microsphere; and

Fig. 12 is a flow chart of the method of the present invention.

Detailed Description of the Preferred Embodiments

A preferred embodiment of the method of the present invention will now be described in reference to Figs. 1a, 1b and 2 of the drawing. According to the present invention, a tissue treatment substance is prepared and includes a chemical agent and a binding agent formulated to

migrate slowly upon injection into tissue. The objective is to allow the chemical agent a lengthened amount of time in contact with the desired treatment area. The substance is injected into the diseased body portion through use of any one of various devices known to those skilled in the art. This is illustrated in Fig. 1a figuratively illustrating injection devices 10, which can be applied to any organ as required. For example, devices that can be used for substance injection are described for use in fluid injection in U.S. Patent Serial Numbers 09/510,537 and 09/105,896. The entire contents of these applications are incorporated in the present disclosure by reference. Another type of device known as a biopsy device can also be used, and is described in the following specification in reference to Fig. 5. A laparoscope device, known to those skilled in the art, can be inserted through an incision for use in guiding an injection needle to a target tissue in the liver 12, kidney 14, uterus 16, bladder 18, and lung 20, of Fig. 1a, as well as other organs not shown. A convenient device for injection into a breast 22 is the apparatus of a biopsy device, with the usual biopsy probe replaced with a hollow core needle. This will be described in reference to Fig. 5. Fig. 1b shows the prostate 24, with a transperineal insertion of a needle. The biopsy device is a convenient tool for this procedure. In guiding a needle to a precise target, the optics of a laparascope or other similar device is often helpful. The use of a non-invasive ultrasound imaging technique is also included in the spirit of the invention for guiding a needle. This is helpful in guiding a biopsy device, and can also be used as an additional optional aid when using a laparascope or similar device. The use of an ultrasound probe and a biopsy device inserted into the rectum for inserting a needle through the rectum wall for injection into the prostate will be described in detail in the following text and drawing.

Preferred forms of the viscous substance include a gel and microspheres. Fig. 2 illustrates the construction of a microsphere 26 with a treatment material 28 captured inside. The microsphere 26 is constructed of a biodegradable material. The gradual deterioration of a plurality of microspheres upon injection provides a slow time release of the treatment material 28.

Fig. 3 illustrates various alternate embodiments of the present invention. A particularly important embodiment includes the application of RF (radio frequency) energy to a target simultaneously with injection of a substance having an electrically conductive property. Fig. 3

shows a biopsy device 30 with an RF input connector 32 for connection of an active side 34 of an RF power supply 36. The device 30 includes construction (not shown) that connects the RF input line 38 electrically to an electrically conductive injection needle 40. The return side 46 of the power supply can also be connected to a connector 32 for making electrical contact with a conductive outer sleeve 42. This is indicated by line 44. Alternatively, device 30 can include one or more additional electrodes 48, insulated from needle 40, and can provide connection of these electrodes with the line 44 to provide localized RF. This approach is known as a bipolar mode of operation. Alternatively, the passive/return side 46 can be connected by a line 50 to a conductive plate 52 positioned at the outside of the body 54. This approach is known as a mono-polar mode of operation. According to the present invention the conductive substance is injected while simultaneously applying RF energy. The result is that the conductive substance serves as an effective electrode extension, and the area of RF energy is concentrated in the volume of tissue 56 infused by the conductive substance. The biopsy device 30 is equipped in this application with a substance injection syringe 58, replacing the conventional biopsy probe. Fig. 3 clearly illustrates a transrectal approach to treating the prostate using an ultrasound imaging device 60, inserted into the rectum 62 for guiding the biopsy probe 42 into the rectum 62 and for guiding the needle 40 into the prostate 64.

The use of a conductive treatment substance in combination with RF energy as illustrated by example in Fig. 3 also applies to any other organ in need of such treatment, particularly including those referred to in reference to Fig. 1a. The construction and use of the various endoscopes, laparoscopes, etc. with RF energy in bipolar or monopolar mode will be understood by those skilled in the art after reading the present disclosure and the incorporated reference applications, including U.S. Patent Application Serial Numbers 09/105,896 and 09/510,537.

Transperineal injection, wherein a needle is inserted percutaneously between the rectum and pubic area into the prostate as shown in Fig. 1b, is further described in detail in Serial Number 09/510,537 in reference to Fig. 17 therein. Transrectal injection of the prostate was discussed above in reference to Fig. 3. Referring now to Fig. 4, a transurethral approach to the prostate is described. An injector apparatus 68 with the aid of a non-invasive imaging device 70, and/or an ultrasonic probe in the rectum as referred to above, is used to inject treatment fluid

into the prostate 66. The apparatus 68 includes an adjustable portion 72 with a scale 74 for extending and retracting a flexible hollow core needle 76, and a syringe apparatus 78 for injection of a substance through the needle 7c. The apparatus 68 is constructed in a similar manner to the apparatus of Fig. 3 in Serial No. 09/510,537 and Fig. 25 in Serial No. 09/105,896. The probe 80 in apparatus 68 differs from the probe 24 of Fig. 3 in Serial No. 09/510,537. Probe 80 is flexible, allowing some conformance to a urethra 82, or other opening as required. The needle 76 is shown bent upward with the tip 84 positioned in the prostate 66. In order to accomplish the bend in the needle, the needle can either be pre-stressed to direct it at an angle upon leaving the probe 80 as described in detail in Serial No. 09/105,896, or a bellows and wire apparatus can be used as described in Serial No. 09/105,896. To incorporate the bellows and wire, an extra sheath employing the bellows and wire can be provided inside the catheter through which the needle extends. Alternatively, the sheath can serve as the catheter. As a further alternative, a larger probe such as probe 24 in Fig. 3 of Serial No. 09/510,537 can be used to incorporate the apparatus described in reference to Figs. 24 and 25 of Serial No. 09/105,896, including the guide wire 293 and sheath 290. The wire tensioning apparatus is described symbolically as item 86 in Fig. 4 of the present disclosure.

An alternate embodiment of the method and apparatus for treating the prostate includes the use of a cystoscope (endoscope), such as endoscope 22 of Fig. 1 in Serial No. 09/510,537, to place the needle near the prostate, and then to use the pretensioned needle or wire and sheath apparatus to direct the needle at an angle. The needle is then extended using the apparatus, with the depth of penetration through the urethra wall and into the prostate monitored through use of a scale, or through use of non-invasive imaging equipment, and/or an ultrasound probe, all as described in U.S. Patent Application Serial No. 09/510,537.

Fig. 4 of the present application also shows a bladder 88 and rectum 90, as examples of organs that can be reached and treated through use of the method of the present invention.

As a further embodiment, a flexible ultrasonic probe can be included inside a catheter, such as catheter 80, or inside the needle 76 of the device shown in Fig. 4. The flexible ultrasonic probe can be inserted inside the needle 76 through an access line as indicated in Fig. 4 by dashed

lines 92 from an ultrasound transceiver 94, entering injector 78 from the side. In the case where the probe is carried alongside the needle 76 in the catheter 80, the flexible probe can be inserted separately, as indicated by lines 96.

Fig. 5 shows further detail of a biopsy device 96, and demonstrates its use in treating a breast 98. the device 96 can also be used according to the present invention to treat the other body organs. A first probe device 100 includes a cannula 102 for puncturing through the skin/tissue as shown. In doing a biopsy, a probe apparatus 104 is inserted through the cannula 102. The biopsy probe 104 has a sharp hook 106 at a distal end for engaging, capturing and retrieving body tissue. According to the present invention, the probe 104 is left out and a hollow core needle 108 is inserted through the cannula 102. The needle 108 is connected to a syringe 110 by way of a Leur hub 112 to a housing 114. The needle 108 can further penetrate the tissue to a required depth 116, and a treatment substance is injected to a volume of tissue 118. For application of RF energy as discussed above, the needle 108 is connected to an RF input connector 120 through housing 114. For monopolar operation, a plate 122 can be placed outside the breast 98 with an RF return line 124 attached and connected to the RF power supply. For bipolar operation, various configurations are possible, as discussed above. For example, the needle 18 can have insulation 126 for electrically separating the conductive needle 108 from the conductive cannula 102. The cannula 102 is electrically attached to a connector 128 for attachment to an electrical return line to the RF power supply. Various alternative arrangements will be apparent to those skilled in the art and are included in the present invention.

Fig. 6 shows the components in a gel for use in the present invention. A gel 130 includes a treatment substance 132 and a binding/gelling agent 134. In addition, a gel can include an electrically conductive element 136, and/or a contrast agent 138.

A list of various treatment substances is given in Fig. 7. A gel or liquid can contain any combination of these or other treatment substances as required and can be used directly as a gel or liquid, or can be enclosed in microspheres. Some of the representative substances can have dual purposes. For example, saline solution and acetic acid are electrically conductive and are therefore also included under the list of conductive substances in Fig. 8. A list of binding/

gelling agents is shown in Fig. 9, and contrast agents are listed in Fig. 10. A contrast agent is a substance that enhances an image. Numerous agents for enhancing an ultrasound image, for example, are well known to those skilled in the art of imaging, and include dyes and various other substances such as barium sulfate, etc. Including a contrast agent in the gel or microspheres enhances the image.

The construction of a microsphere 140 as a substance for use in the present invention is more clearly illustrated in reference to Fig. 11. A sealed container 142 is shown in cross section, and can have any shape i.e. oval, cylindrical, etc., and with its contents will be referred to generally as a microsphere. The purpose of the microsphere 140 is to carry a substance 144 to a target tissue, and through gradual absorption/disintegration of the container 142, will provide a corresponding gradual release of the treatment substance 144. The microsphere 140 also does not migrate/diffuse as rapidly as a liquid, and therefore allows more control of the area/volume of tissue being treated. The substance 144 can be a gel 146 with elements selected as discussed in reference to Figs. 6-9, or it can be a liquid 148 with similar components including a treatment substance 150 and as required/desired a conductive material 152 and/or a contrast agent 154. The microsphere 140 also preferably contains a gas 156 which can be any of various gasses, such as air, helium, fluorocarbons, etc. as noted in block 158. The microsphere container 142 and contents 144 and 156 are formed by combining a biomaterial or biodegradable polymer 160 (for forming the wall 142) with the substance 144 along with the gas 156 in a pressurized form. The details of such a process are well known to those skilled in the art and need not be described in detail herein.

The microsphere 140 structure also provides echogenic enhancement/image enhancement during ultrasound imaging. The gas 156 and substance 144 do not mix well, and the two materials (gas vs. gel/liquid) reflect sound differently, which creates a recognizable reflection/image of the substance and therefore area of treatment. As noted above, the substance 144 can also include an image enhancement component.

The preferred method of the present invention will now be described in reference to the flow chart of Fig. 12. A hollow core needle, or probe and hollow core needle or catheter is/are

inserted into a patient's body (block 162) through an appropriate opening, such as an incision, or through a natural passageway such as a urethra or cervical canal, rectum, etc. If a catheter or probe is used, the hollow core needle can be inserted through the probe or catheter either before or after insertion of the probe or catheter in the body. Through use of an endoscope, and/or a non-invasive detection positioning and imaging method, for example using ultrasound, etc., the user accurately positions the needle near a site to be treated (block 164). Having arrived near the target area, either an endoscope and/or non-invasive detection and imaging methods such as X-RAY, CT SCAN, MRI, ultrasound, fluoroscopy, etc. can be used to guide the needle or an appropriate needle assembly to a target area to be treated, and to monitor injection of the treatment substance. The needle assembly can be solely for application or injection of a substance to a precise target tissue location, or it can be additionally for application of RF energy.

In the case when RF energy is to be applied to the needle(s), the needle(s) are electrically conductive. The RF application can be monopolar wherein the energy is applied to one or more needles and an electrical return path is provided through a conductor placed exterior of the body, such as a conductive plate with a conductor line attached to the energy power supply return. Alternatively, the energy can be applied in a bipolar mode, wherein an electrical return path is provided locally, inside the body and near the needle/probe, etc. used to carry the RF energy into the body. The substance can be of a single type or a combination of substances, and as described above, and can be in the form of a gel, semi-liquid, a suspension, foam, viscous biomaterial or microsphere. The substance can include an electrically conductive component, or the substance can be non-conductive. In the embodiment wherein RF energy is transmitted along the needle while injecting an RF conductive substance, the substance serves as an effective extension of the needle/electrode providing enhanced RF energy application to the volume of tissue penetrated by the substance.

According to the method of the present invention, the needle is used either to apply a substance to a tissue surface, or is advanced interstitially into body tissue in need of treatment (block 164), the needle depth being observed by use of any of various methods, such as those listed including an endoscope for viewing marks on the needle, etc., a scale on the injector or

probe handle, or noninvasive imaging and position detection using X-RAY, CT scan, fluoroscopy, ultrasound etc.

For the purpose of the present disclosure, a non-invasive imaging technique is defined as any technique that allows observation of tissue or structure such as a needle in tissue without the use of additional invasive equipment for providing a view using visual light, such as the use of an endoscope or actual cutting away of tissue for a direct view. An ultrasound probe, for example, could be inserted by any means, through a natural opening, or through an incision to a point of interest, and then could provide a non-invasive view of an area beyond the probe through use of ultrasound imaging equipment. This use is termed non-invasive in the present disclosure.

The preferred embodiment of the invention includes an apparatus and method for directing a needle to a target area by bending the needle. This is particularly useful in the application wherein a flexible needle assembly is passed inside a catheter through a urethra to the vicinity of a prostate. A needle guiding apparatus is then used to deflect the needle tip toward the specific target area in the prostate.

With the needle tip at the target tissue, the treatment substance is injected (block 166) into the specific target tissue without affecting the surrounding area. The method can also, as an alternative/optional embodiment, include the application of RF energy upon injection of the substance. The substance can be either conductive or non-conductive. In the embodiment wherein the substance is conductive, the RF energy travels along the needle to the needle tip, and then continues to pass through the conductive substance acting as an extension of the needle/electrode and enhancing the RF energy in the volume of tissue treated by the substance. The application of RF energy can be for either causing hyperthemia or for causing tissue necrosis. Upon completion of treatment of the selected volume, the needle is removed from the treatment site (block 168).

At this point the apparatus can be either removed, or a new site in need of treatment can be identified and therapy applied. The process of identification is indicated by block 170. In the case where an endoscope is used, with or without the aid of observation with X-RAY, CT scan,

fluoroscopy or ultrasound, the probe can be moved to observe additional tissue to determine further areas in need of treatment. If observation is limited to X-RAY, CT scan, fluoroscopy, ultrasound, these tools are used alone to determine any additional targeted treatment areas. In either of the tool combinations noted above, they are used to precisely locate the targeted treatment area, place and/or insert the needle to the desired depth, and observe the substance flow and effect on the tissue. If no further treatment is required, the probe, needle assembly, and endoscope (if present) are removed (block 172). If further treatment is required, the probe and needle are positioned accordingly (block 164) and the needle is used to apply the substance to the tissue surface, or it is advanced into the tissue, and a sufficient volume of the substance is injected (block 166).

In applications for destruction/death of tissue, the necrossing agent can be combined with carrier agents and/or an anesthetic agent and/or with an antibiotic. Anesthetic agents, for example, include Lidocaine, Markaine and Sensorcaine as listed in Fig. 7, and other anesthetic agents known by those skilled in the art. Similarly, antibiotic agents include the various products known in the art.

The method of the present invention also has a significant advantage in gene therapy. In this case the application of RF energy for causing tissue death is generally not applicable. However, a smaller amount of RF energy can be applied for the purpose of raising the tissue temperature, i.e. creating hyperthermia to enhance a process. The prior art method of gene delivery injects genes into the body intravenously or intra-arterially using a conventional needle. This distributes the genes throughout the body. Ideally, the genes should be confined to the target area. Genes are listed in Fig. 7, as are other substances that for many illnesses, such as the treatment of tumors, should optimally be injected directly into the tumor or other target tissue. These include viruses, vaccines, proteins, tumor suppression genes, inhibitors, markers, and other biological agents. The substances that can be used in accordance with the therapy of the present invention also include mixtures of the above listed items and other chemicals, agents and their solutions in the form of gel, or suspensions, liquids or semi-liquids in microspheres that will be understood by those skilled in the art.

The method of Fig. 12 according to the present invention is meant to cover treatment of any body part. A most important embodiment is the method of the present invention applied to causing selective tissue necrosis, with or without the application of RF energy. Preferred embodiments of the present invention include treatment of the prostate, kidney, uterine myoma, fibroids, liver, ovarian cancer, bladder cancer, breast tumors and cysts (benign or malignant), and stomach, lung, colon and brain cancer, etc., and in the procedure of endometrial ablation of the uterine lining. An important embodiment in use with male patients is treatment of BPH (benign Prostatic Hyperplenia), enlarged prostate growth and prostate cancer. In this case, the needle can be inserted transurethrally, transrectally, or transperineally with or without an incision. The probe can also be inserted transperineally or transrectally (through the rectum) with or without incision under imaging guidance.

The method of the present invention is not limited to using the endoscope apparatus discussed herein and in Serial Nos. 09/105,896 and 09/510,537. Any type of scope apparatus that can be used to guide a needle to a target area is applicable to the method, such as cystoscopes, endoscopes, hysteroscopes, laparoscopes, bronchoscopes, gasteroscopes, etc. As mentioned above, a biopsy apparatus can also be used.

Although the present invention has been described above in terms of a specific embodiment, it is anticipated that alterations and modifications thereof will no doubt become apparent to those skilled in the art. It is therefore intended that the following claims be interpreted as covering all such alterations and modifications as fall within the true spirit and scope of the invention.

WHAT IS CLAIMED IS:

CLAIMS

1. A method for treating a localized portion of body tissue comprising:

(a) inserting a needle apparatus in a body, said apparatus including at least one hollow core needle for delivering a treatment substance into said body;

(b) guiding said needle apparatus to a target tissue in need of treatment, and said guiding including use of an imaging technique for viewing inside an area of tissue; and

(c) applying said treatment substance to said target tissue through said needle apparatus;

wherein said treatment substance includes a component selected from the group consisting of tissue necrosis agents, genes, viruses, proteins, inhibitors, tissue markers, bioabsorbable polymers and other biological agents and chemotherapeutic agents.

2. A method as recited in claim 1 wherein said method is for causing selective tissue necrosis.

3. A method as recited in claim 1 wherein said treatment substance is in the form of a gel.

4. A method as recited in claim 1 wherein said treatment substance is in the form of microspheres.

5. A method for treating a localized portion of body tissue comprising:

(a) inserting a needle apparatus in a body, said apparatus including at least one hollow core needle for delivering a treatment substance into said body;

(b) guiding said needle apparatus to a target tissue in need of treatment; and

(c) applying said treatment substance to said target tissue through said needle apparatus;

wherein said treatment substance includes a plurality of microspheres including a component selected from the group consisting of tissue necrosing agents, genes, viruses, proteins, inhibitors, tissue markers, bioabsorbable polymers and other biological agents and chemotherapeutic agents.

6. A method as recited in claim 5 wherein said method is for causing selective tissue necrosis.

7. A method for treating a localized portion of body tissue comprising:

(a) inserting a needle apparatus in a body, said apparatus including at least one hollow core needle for delivering a treatment gel into said body;

(b) guiding said needle apparatus to a target tissue in need of treatment; and

(c) applying said treatment gel to said target tissue through said needle apparatus;

wherein said treatment gel includes at least one component selected from the group consisting of tissue necrosing agents, genes, viruses, proteins, inhibitors, tissue markers, bioabsorbable polymers and other biological agents and chemotherapeutic agents.

8. A method as recited in claim 7 wherein said method is for causing selective tissue necrosis.

9. A method as recited in claim 1 further comprising applying RF energy to said target tissue through an RF electrode.

10. A method as recited in claim 9 wherein said substance includes an electrically conductive component.

11. A method as recited in claim 5 further comprising applying RF energy to said target tissue through an RF electrode.

12. A method as recited in claim 11 wherein said microspheres include an electrically conductive agent.

13. A method as recited in claim 7 further comprising applying RF energy to said target tissue through an RF electrode.

14. A method as recited in claim 13 wherein said gell includes an electrically conductive agent.

15. A method as recited in claim 1 wherein said substance includes an image contrasting agent.

16. A method as recited in claim 5 wherein said guiding includes use of an imaging technique.

17. A method as recited in claim 16 wherein said microspheres include an image contrasting agent.

18. A method as recited in claim 7 wherein said guiding includes use of an imaging technique.

19. A method as recited in claim 18 wherein said gel includes an image contrasting agent.

20. A method as recited in claim 16 wherein each said microsphere includes a container holding therein a gas and a substance selected from the group consisting of a gel and a liquid for providing image enhancement when said imaging technique is ultrasound.

21. A method as recited in claim 1 wherein said target tissue is in a prostate, and wherein said method is for treating a condition selected from the group consisting of BPH and prostate cancer, and wherein said inserting is accomplished by a method selected from the group consisting of Transrectal, Transurethral and Transperineal approach.

22. A method as recited in claim 5 wherein said target tissue is in a prostate, and wherein said method is for treating a condition selected from the group consisting of BPH and prostate cancer, and wherein said inserting is accomplished by a method selected from the group consisting of Transrectal, Transurethral and Transperineal approach.

23. A method as recited in claim 7 wherein said target tissue is in a prostate, and wherein said method is for treating a condition selected from the group consisting of BPH and prostate cancer, and wherein said inserting is accomplished by a method selected from the group consisting of Transrectal, Transurethral and Transperineal approach.

24. A method as recited in claim 1 wherein said method is applied for the treatment of a body part selected from group consisting of prostate, liver, uterus, bladder, kidney, lung, and breast.

25. A method as recited in claim 24 wherein said inserting is accomplished using an approach selected from the group consisting of percutaneous, laparoscopic, and endoscopic.

26. A method as recited in claim 5 wherein said method is applied for the treatment of a body part selected from group consisting of prostate, liver, uterus, bladder, kidney, lung, and breast.

27. A method as recited in claim 26 wherein said inserting is accomplished using an approach selected from the group consisting of percutaneous, laparoscopic, and endoscopic.

28. A method as recited in claim 7 wherein said method is applied for the treatment of a body part selected from group consisting of prostate, liver, uterus, bladder, kidney, lung, and breast.

29. A method as recited in claim 28 wherein said inserting is accomplished using an approach selected from the group consisting of percutaneous, laparoscopic, and endoscopic.

30. A method as recited in claim 1 wherein said guiding is further performed using a device selected from the group consisting of biopsy apparatus, laparoscope, endoscope, hysteroscope, MRI, CT scan, and ultrasound imaging apparatus.

31. A method as recited in claim 5 wherein said guiding is performed using a device selected from the group consisting of biopsy apparatus, laparoscope, endoscope, hysteroscope, MRI, CT scan, and ultrasound imaging apparatus.

32. A method as recited in claim 7 wherein said guiding is performed using a device selected from the group consisting of biopsy apparatus, laparoscope, endoscope, hysteroscope, MRI, CT scan, and ultrasound imaging apparatus.

33. A method as recited in claim 1 wherein said inserting is performed by at least one method selected from the group consisting of percutaneous, through an incision, and through a natural body opening, and a laparoscopic approach.

34. A method as recited in claim 5 wherein said inserting is performed by at least one method selected from the group consisting of percutanious, through an incision, and through a natural body opening.

35. A method as recited in claim 7 wherein said inserting is performed by at least one method selected from the group consisting of percutanious, through an incision, and through a natural body opening, and a laparoscopic approach.

36. A method as recited in claim 4 wherein said microspheres further include a chemo agent selected from the group consisting of hypertonic saline solution, ethanol, acetic acid, and other necrosing agents.

37. A method as recited in claim 7 wherein said gel further includes a chemo agent selected from the group consisting of hypertonic saline solution, acetic acid, ethanol and other tissue necrosing agents, and wherein said gel further includes a binding agent.

38. A method as recited in claim 5 wherein each said microsphere further includes a gas.

39. A method as recited in claim 38 wherein said gas is selected from the group consisting of air, helium, fluorocarbon, and carbon dioxide.

40. A method as recited in claim 37 wherein said binding agent is selected from the group consisting of biomaterial, polymer, biodegradable polymer, a suspension agent, a derivative of a protein, fat, collagen, and oil.

41. A method as recited in claim 1 wherein said conductive substance is selected from the group consisting of conductive polymers, conductive agents, conductive elements, carbon particles, and metallic suspensions.

ABSTRACT

A method wherein a viscous treatment substance is injected into a diseased portion of body tissue for the purpose of localizing tissue necrosis by resisting substance migration. The treatment substance injected is in the form of a gel, or alternatively in the form of microspheres. Localized treatment is further enhanced by including a conductive component in the treatment substance, and while injecting the substance, simultaneously applying RF (radio frequency) energy to an injection needle acting as an RF electrode. The conductive gel serves as an extension of the electrode, thereby localizing and enhancing treatment in the tissue penetrated by the gel. Improved positioning of the injection needle is aided with the use of ultrasound imaging with clarity enhanced by inclusion of imaging enhancement agents in the gel. Alternatively, microspheres are filled with a gel/solution and gas combination providing contrasting areas of ultrasound reflection.

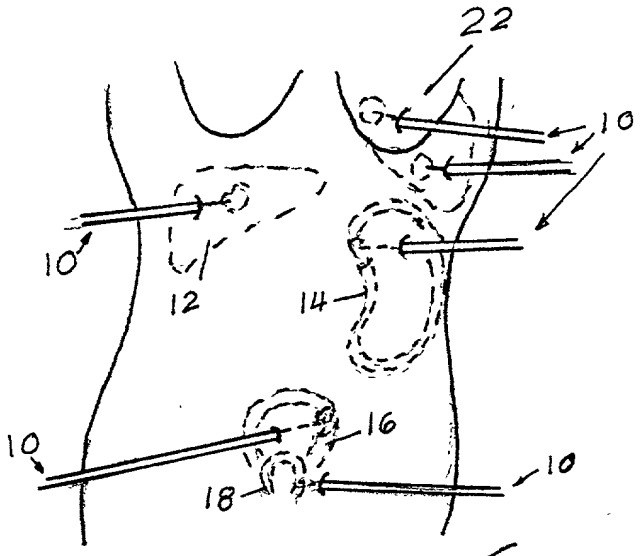

FIG. 1a

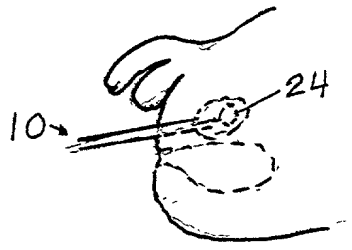

Fig. 1b

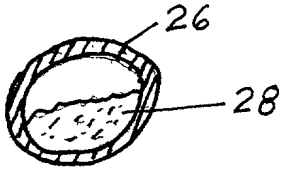

FIG. 2

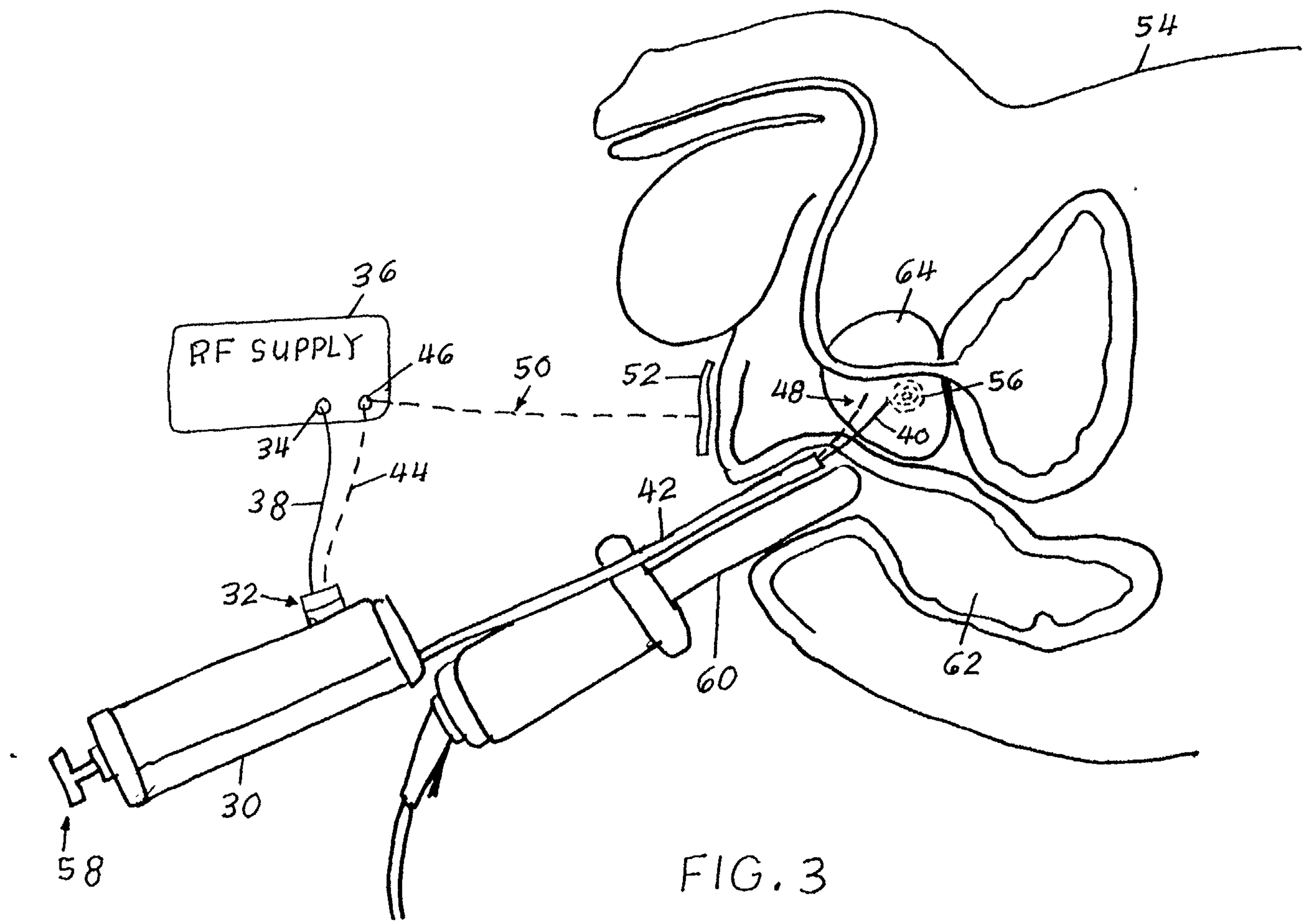

FIG. 3

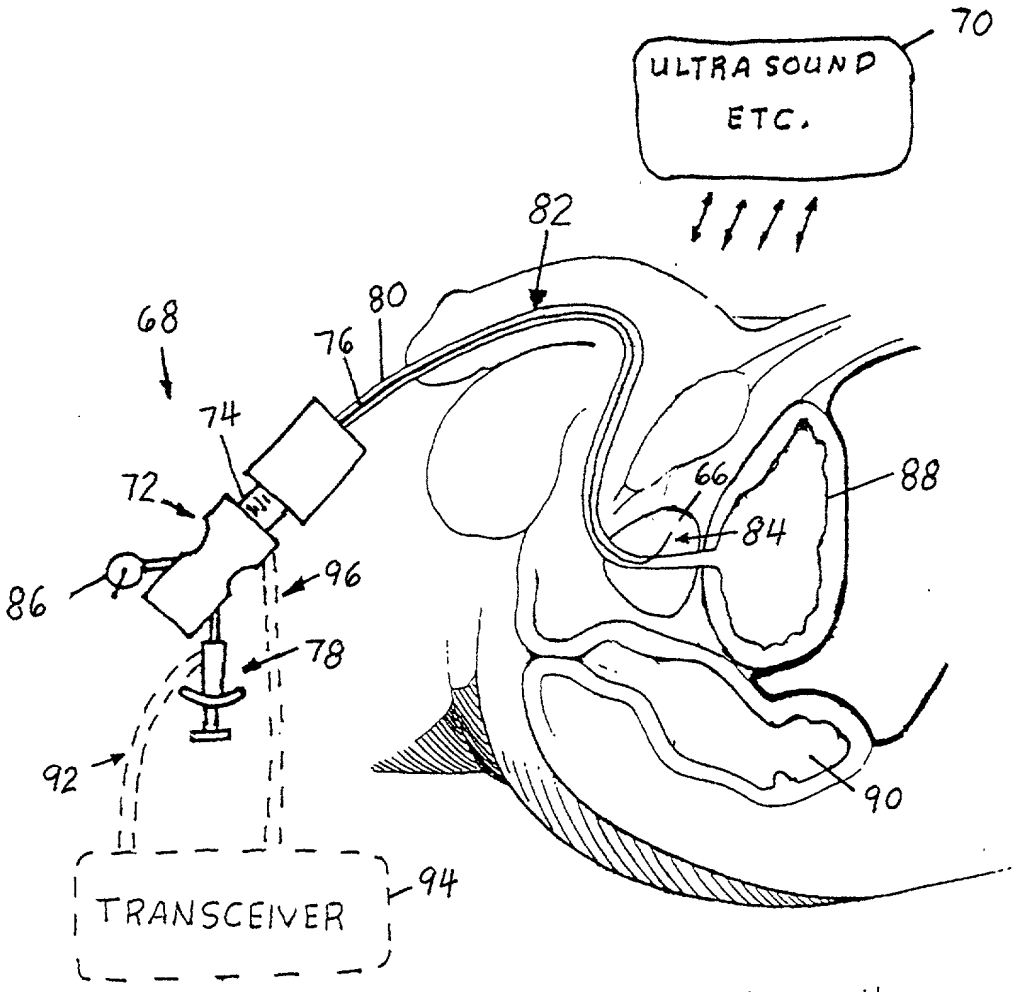
ULTRA SOUND
ETC.
70
82
80
68
76
74
72
86
96
78
92
94
TRANSCEIVER
66
84
88
90

FIG. 4

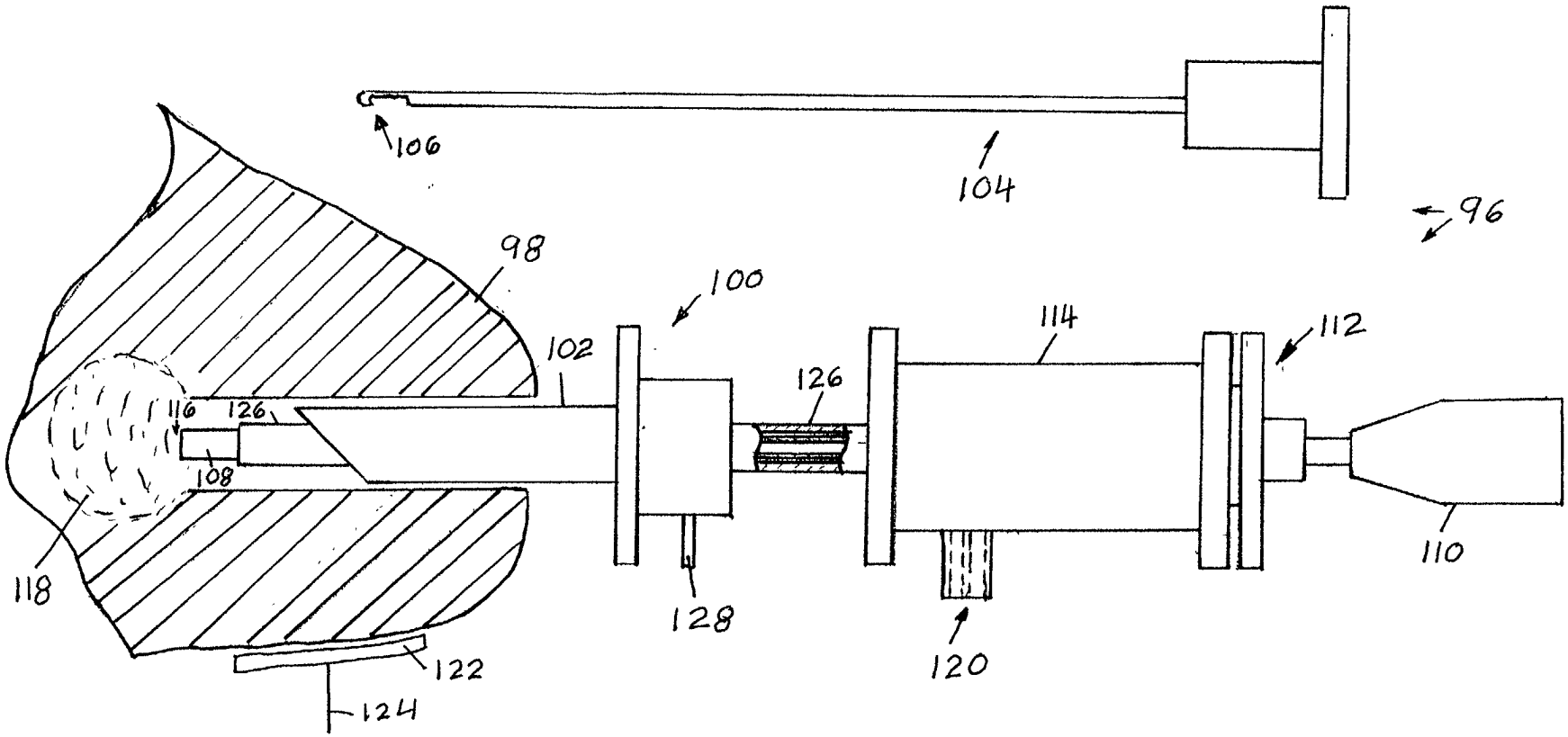

FIG. 5

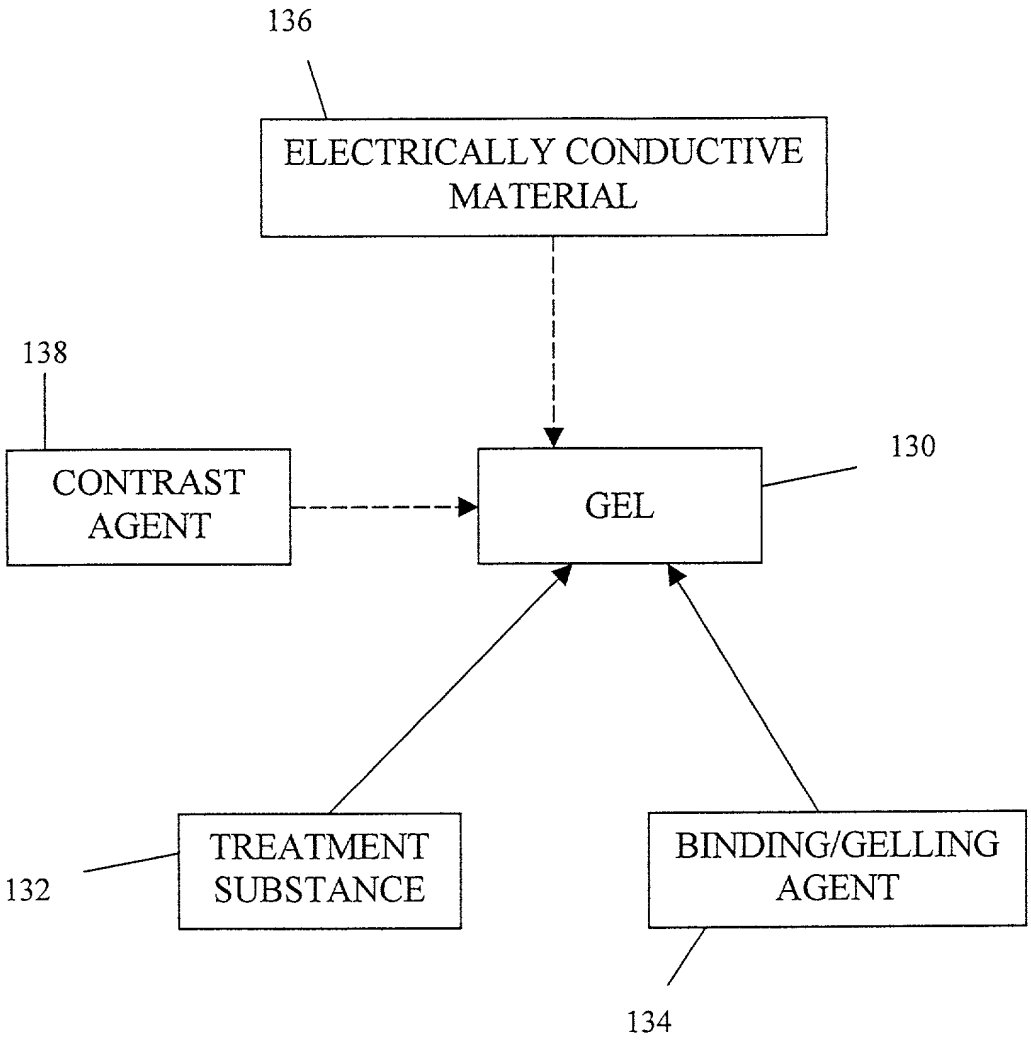
136
ELECTRICALLY CONDUCTIVE MATERIAL
138
CONTRAST AGENT
GEL
130
TREATMENT SUBSTANCE
132
BINDING/GELLING AGENT
134

FIG. 6

THERAPY SUBSTANCES

- NECROSSING AGENTS
  - ETHANOL ALCOHOL (1% TO 100% PURE)
  - SALINE SOLUTION (0.9% TO 99%)
  - ACETIC ACID (1% TO 100%)
  - NATURAL EXTRACTS / COMPOUNDS
  - ENZYMES

- ANESTHETIC AGENTS
  - LIDOCAINE
  - MARKAINE
  - SENSORCAINE
- ANTIBIOTICS
- GENES
- VIRUS
- VACCINES
- PROTEINS
- TUMOR SUPPRESSION GENES
- INHIBITORS
- TISSUE MARKERS
- OTHER BIOLOGICAL AGENTS
- BIOABSORBABLE POLYMERS
- POLYMERS WITH CHEMOTHERAPEUTIC AGENTS AND PHARMACEUTICAL DRUGS

FIG. 7

ELECTRICALLY CONDUCTIVE MATERIAL

- SALINE SOLUTION (ISOTONIC OR HYPERTONIC)
- ACETIC ACID
- ETHANOL
- OTHER, ETC.
- CONDUCTIVE POLYMER
- METALLIC SUSPENSION
- CARBON PARTICLE
- CONDUCTIVE ELEMENT

FIG. 8

BINDING/GELLING AGENTS

1. Polymers
   - i) hydroxyl propyl cellulose
   - ii) hydroxyl propyl methyl cellulose
   - iii) hydroxyl propyl ethyl cellulose
   - iv) poly vinyl alcohol
2. Biodegradable polymer
3. Bio-material
4. Oil and Animal Fat Based Biomaterial and Agents
5. Collagen-Natural Derivatives and Synthetic Formulations
6. Phase Changing Gelling Agents
7. Energy Activated Gelling Agents
8. Proteins, Conjugates and Tissue Cell Compositions

FIG. 9

CONTRAST AGENT

- **DYE**
- **BARIUM SULFATE**
- **OTHER**

FIG. 10

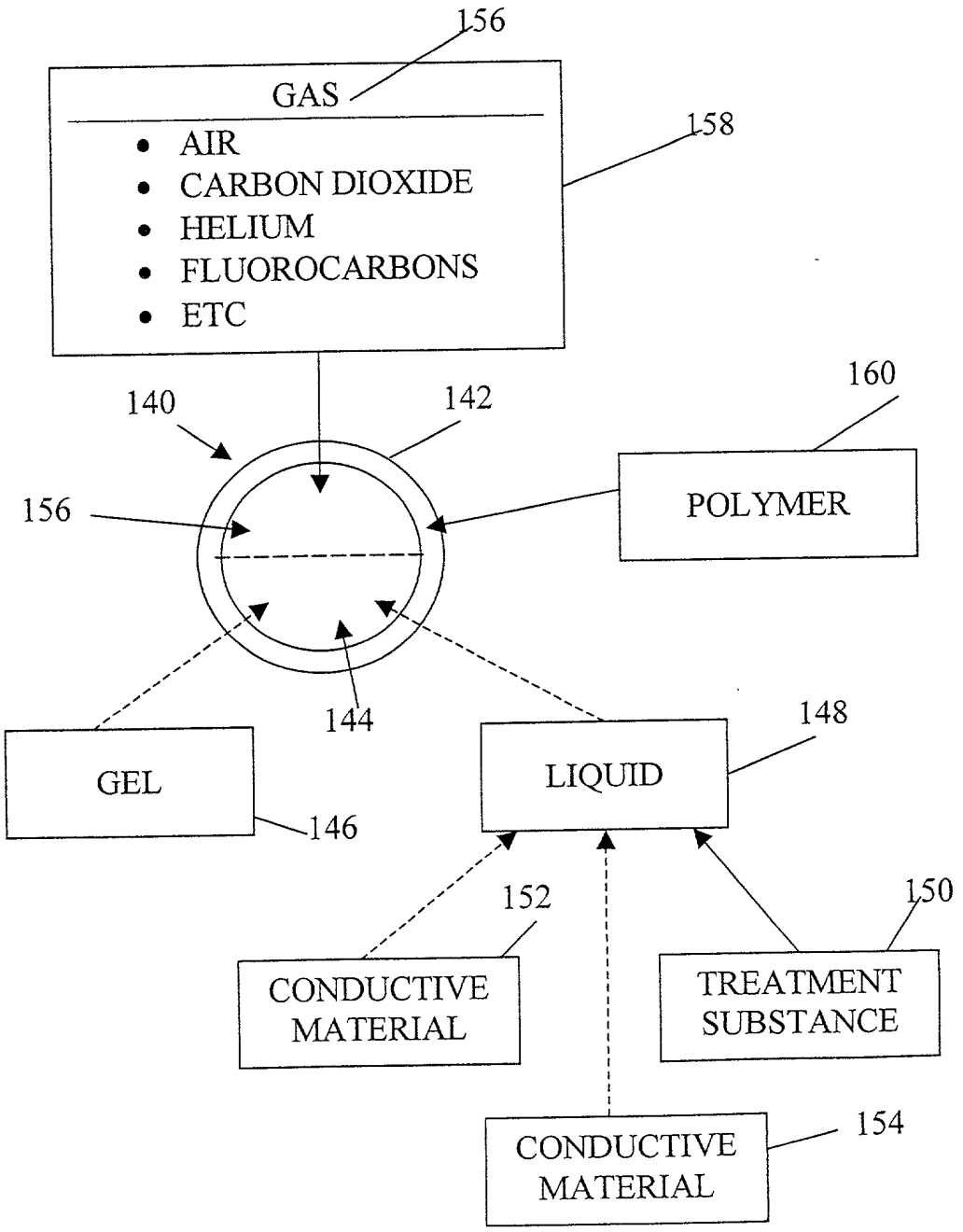

FIG. 11

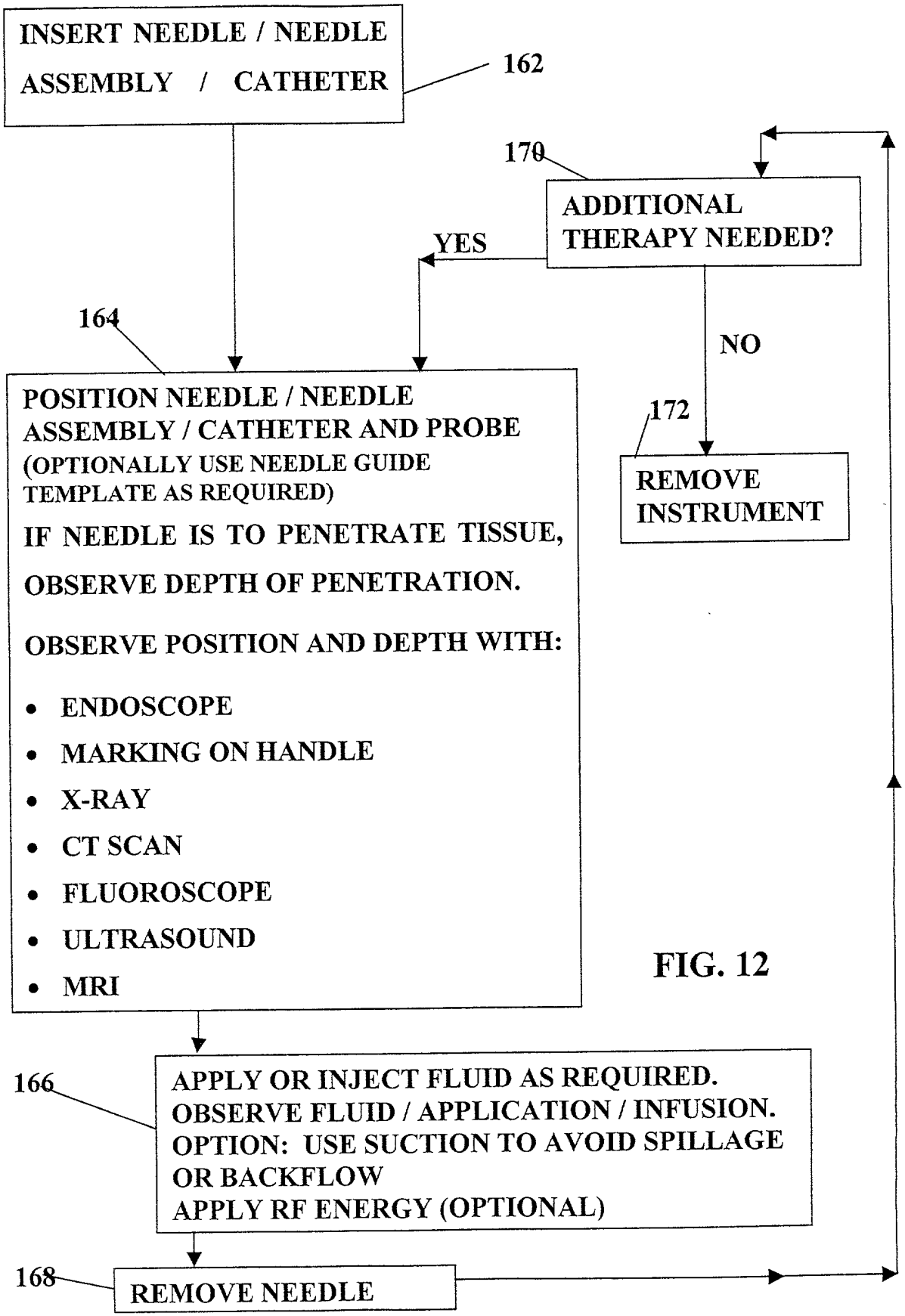
INSERT NEEDLE / NEEDLE ASSEMBLY / CATHETER
162
170
ADDITIONAL THERAPY NEEDED?
YES
NO
164
POSITION NEEDLE / NEEDLE ASSEMBLY / CATHETER AND PROBE
(OPTIONALLY USE NEEDLE GUIDE TEMPLATE AS REQUIRED)
IF NEEDLE IS TO PENETRATE TISSUE,
OBSERVE DEPTH OF PENETRATION.
OBSERVE POSITION AND DEPTH WITH:
• ENDOSCOPE
• MARKING ON HANDLE
• X-RAY
• CT SCAN
• FLUOROSCOPE
• ULTRASOUND
• MRI
172
REMOVE INSTRUMENT
166
APPLY OR INJECT FLUID AS REQUIRED.
OBSERVE FLUID / APPLICATION / INFUSION.
OPTION: USE SUCTION TO AVOID SPILLAGE OR BACKFLOW
APPLY RF ENERGY (OPTIONAL)
168
REMOVE NEEDLE

FIG. 12

RULE 63 (37 C.F.R. 1.63)
DECLARATION AND POWER OF ATTORNEY FOR PATENT APPLICATION
IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

As a below named inventor, I hereby declare that my residence, post office address and citizenship are as stated below next to my name, and I believe I am an original, first and joint inventor of the subject matter which is claimed and for which a patent is sought on the invention entitled **Method for Tissue Treatment with Injected Substance**, the specification of which was filed in the U.S. Patent Office on November 17, 2000 under Serial No._____.

I hereby state that I have reviewed and understand the contents of the above identified specification, including the claims, as amended by any amendment referred to above. I acknowledge the duty to disclose all information known to me to be material to patentability as defined in 37 C.F.R. 1.56. I hereby claim foreign priority benefits under 35 U.S.C. 119/365 of any foreign application(s) for patent or inventor's certificate listed below and have also identified below any foreign application for patent or inventor's certificate filed by me or my assignee disclosing the subject matter claimed in this application and having a filing date (1) before that of the application on which priority is claimed, or (2) if no priority claimed, before the filing date of this application:

PRIOR FOREIGN APPLICATION(S): Number	Country	Day/MONTH/Year Filed	Date first Laid-open or Published	Date Patented or Granted	Priority Claimed
					Yes ☐ No ☐

I hereby claim domestic priority benefit under 35 U.S.C. 119/120/365 of the indicated United States applications listed below and PCT international applications listed above or below and, if this is a continuation-in-part (CIP) application, insofar as the subject matter disclosed and claimed in this application is in addition to that disclosed in such prior applications, I acknowledge the duty to disclose all information known to me to be material to patentability as defined in 37 C.F.R. 1.56 which became available between the filing date of each such prior application and the national or PCT international filing date of this application:

PRIOR U.S. PROVISIONAL, NONPROVISIONAL AND/OR PCT APPLICATION(S) Application No.:	Day/MONTH/Year Filed:	Status pending, abandoned, patented)	Priority Claimed?
09/519,937	**February 22, 2000**	**pending**	Yes ☑ No ☐
08/105,896	**June 26, 1998**	**pending**	Yes ☑ No ☐
08/639,199	**April 26, 1996**	**now 5,861,002**	Yes ☑ No ☐
08/259,712	**June 14, 1994**	**now 5,562,703**	Yes ☑ No ☐
08/025,003	**March 2, 1993**	**abandoned**	Yes ☑ No ☐
07/779,108	**October 18, 1991**	**now 5,322,503**	Yes ☑ No ☐

and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

And I hereby appoint Pillsbury Madison & Sutro LLP, 1100 New York Avenue, N.W., Ninth Floor, East Tower, Washington, D.C. 20005-3918, telephone number (650) 233-4790 (to whom all communications are to be directed), and the below-named persons (of the same address) individually and collectively my attorneys to prosecute this application and to transact all business in the Patent and Trademark Office connected therewith and with the resulting patent, and I hereby authorize them to delete persons no longer with their firm and to act and rely on instructions from and communicate directly with the person/assignee who first sent this case to them and by whom I hereby declare that I have consented after full disclosure to be represented unless/until I instruct the above Firm and/or a below attorney in writing to the contrary.

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G. Lloyd Knight	17698	Kendrew H. Colton	30368	Paul F. McQuade	31542	Adam R. Hess	41835
Carl G. Love	18781	Paul E. White, Jr.	32011	Ruth N. Morduch	31044	William P. Atkins	38821
Kevin E. Joyce	20508	G. Paul Edgell	24238	Richard H. Zaitlen	27248	Paul L. Sharer	36004
George M. Sirilla	18221	Lynn E. Eccleston	35861	Roger R. Wise	31204	DAVID H. JAFFER	32243
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